

APPLICANT: Stanley T. Crooke
SERIAL NO: 09/479,783

DOCKET NO: ISIS-4313 (ISIS0002-102)

AMENDMENTS TO THE CLAIMS: This listing of claims replaces all prior versions and listings of claims in the instant patent application.

Listing of claims:

1-77. (Canceled).

78. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides are not covalently linked, wherein each of said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said ~~duplex~~; duplex, and wherein at least one of said first and said second oligonucleotides having has portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases, ~~and wherein each of said first and said second oligonucleotides comprises a nucleotide sequence consisting from eight to fifty nucleoside subunits.~~

79. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides are not covalently linked, wherein each of said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said ~~duplex~~; duplex, and wherein at least one of said first and said second oligonucleotides having has portions flanking said central portions having chemical modifications which make them resistant to single-stranded nucleases and increase their affinity for the other oligonucleotide of the duplex.

80. (Previously presented) The composition of claim 78, wherein said chemical modifications are phosphorothioate linkages or 2'-methoxy modifications.

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81. (Previously presented) An affinity matrix comprising the composition of claim 78.

82-92. (Canceled).

93. (Previously presented) A composition of claim 78, wherein one of said oligonucleotides has the nucleotide sequence of SEQ ID NO: 8.

94. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides are not covalently linked, wherein each of said first and second oligonucleotides include a portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages and wherein said portions are base-paired with each other in said duplex, and wherein at least one of said first and said second oligonucleotides includes chemical modifications that make said oligonucleotide resistant to single-stranded nucleases ~~each of said first and said second oligonucleotides comprises a nucleotide sequence consisting from eight to fifty nucleoside subunits.~~

95. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides are not covalently linked, wherein each of said first and second oligonucleotides include a portion having at least four consecutive ribofuranosyl residues that are base-paired with each other in said ~~duplex; duplex, and wherein~~ at least one of said first and said second oligonucleotides ~~including~~ includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases, ~~and wherein each of said first and said second oligonucleotides comprises a nucleotide sequence consisting from eight to fifty nucleoside subunits.~~

96. (Canceled)

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97. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides are not covalently linked, wherein each of said first and second oligonucleotides include a portion having at least four consecutive ribofuranosyl residues, wherein and where said portions are base paired with each other in said ~~duplex~~, and duplex, and wherein at least one of said first and second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases and that increases the affinity for said oligonucleotide for the other of said oligonucleotides.

98-105. (Canceled).

106. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said ~~duplex~~; duplex, wherein at least one of said first and said second oligonucleotides ~~having~~ has portions flanking said central portions, said portions having chemical modifications which make them resistant to single-stranded nucleases, and wherein one of said oligonucleotides has the nucleotide sequence of SEQ ID NO: 8.

107-116. (Canceled).

117. (Previously presented) The composition of claim 78 wherein said chemical modifications are phosphorothioate linkages.

118. (Previously presented) The composition of claim 78 wherein said chemical modifications are 2'-methoxy modifications.

119. (Previously presented) The composition of claim 78 wherein said chemical modifications are 2'-fluoro modifications.

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120. (Previously presented) The composition of claim 78 wherein said chemical modifications are 2'-O-methoxyethoxy modifications.

121. (Currently amended) The composition of claim 78 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

122. (Currently amended) The composition of claim 78 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

123. (Previously presented) The composition of claim 79 wherein said chemical modifications are phosphorothioate linkages.

124. (Previously presented) The composition of claim 79 wherein said chemical modifications are 2'-methoxy modifications.

125. (Previously presented) The composition of claim 79 wherein said chemical modifications are 2'-fluoro modifications.

126. (Previously presented) The composition of claim 79 wherein said chemical modifications are 2'-O- methoxyethoxy modifications.

127. (Currently amended) The composition of claim 79 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

128. (Currently amended) The composition of claim 79 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

129. (Previously presented) The composition of claim 94 wherein said chemical modifications are phosphorothioate linkages.

130. (Previously presented) The composition of claim 94 wherein said chemical modifications are 2'-methoxy modifications.

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131. (Previously presented) The composition of claim 94 wherein said chemical modifications are 2'-fluoro modifications.

132. (Previously presented) The composition of claim 94 wherein said chemical modifications are 2'-O- methoxyethoxy modifications.

133. (Currently amended) The composition of claim 94 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

134. (Currently amended) The composition of claim 94 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

135. (Previously presented) The composition of claim 95 wherein said chemical modifications are phosphorothioate linkages.

136. (Previously presented) The composition of claim 95 wherein said chemical modifications are 2'-methoxy modifications.

137. (Previously presented) The composition of claim 95 wherein said chemical modifications are 2'-fluoro modifications.

138. (Previously presented) The composition of claim 95 wherein said chemical modifications are 2'-O- methoxyethoxy modifications.

139. (Currently amended) The composition of claim 95 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

140. (Currently amended) The composition of claim 95 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

141-146. (Canceled).

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147. (Previously presented) The composition of claim 97 wherein said chemical modifications are phosphorothioate linkages.

148. (Previously presented) The composition of claim 97 wherein said chemical modifications are 2'-methoxy modifications.

149. (Previously presented) The composition of claim 97 wherein said chemical modifications are 2'-fluoro modifications.

150. (Previously presented) The composition of claim 97 wherein said chemical modifications are 2'-O- methoxyethoxy modifications.

151. (Currently amended) The composition of claim 97 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

152. (Currently amended) The composition of claim 97 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

153-175. (Canceled)

176. (Previously presented) The composition of claim 106 wherein said chemical modifications are phosphorothioate linkages.

177. (Previously presented) The composition of claim 106 wherein said chemical modifications are 2'-methoxy modifications.

178. (Previously presented) The composition of claim 106 wherein said chemical modifications are 2'-fluoro modifications.

179. (Previously presented) The composition of claim 106 wherein said chemical modifications are 2'-O- methoxyethoxy modifications.

180. (Currently amended) The composition of claim 106 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is twelve to thirty nucleoside subunits in length.

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181. (Currently amended) The composition of claim 106 wherein one of said first and said second oligonucleotides ~~comprises a nucleotide sequence consisting from~~ is fifteen to twenty-five nucleoside subunits in length.

182. (New) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is about 17 to about 20 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides comprises chemical modifications that increase its resistance to single-stranded nucleases.

183. (New) The composition of claim 182 wherein said portions have phosphodiester linkages.

184. (New) The composition of claim 182 wherein the chemical modifications are 2'-methoxy modifications.

185. (New) The composition of claim 182 wherein the chemical modifications are 2'-fluoro modifications.

186. (New) The composition of claim 182 wherein the chemical modifications are 2'-O-methoxyethoxy modifications.

187. (New) The composition of claim 182 wherein the chemical modifications are phosphorothioate linkages.

188. (New) The composition of claim 182 wherein at least one oligonucleotide further comprises at least one chemical modification that increases its affinity for the other oligonucleotide.

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189. (New) The composition of claim 182 wherein at least of one of said first and said second oligonucleotides is 17 nucleobase subunits in length.

190. (New) The composition of claim 189 wherein each of said first and said second oligonucleotides is 17 nucleobase subunits in length.

191. (New) The composition of claim 182 wherein at least of one of said first and said second oligonucleotides is 20 nucleobase subunits in length.

192. (New) The composition of claim 189 wherein each of said first and said second oligonucleotides is 20 nucleobase subunits in length.

193. (New) The composition of claim 182 which activates a double-stranded RNA nuclease.